RECOMMENDATIONS FOR THE PREVENTION AND CONTROL OF INFLUENZA OUTBREAKS IN CALIFORNIA LONG-TERM CARE FACILITIES, 1999/2000

These recommendations were developed by the California Department of Health Services, Division of Communicable Disease Control, using information from the Centers for Disease Control and Prevention, in consultation with the Licensing and Certification Program, and are revised annually. This information is intended to be advisory only and was developed to assist facility infection control committees in the development of a rational approach to the prevention and control of influenza outbreaks in long-term healthcare facilities.

What Is Influenza?

Influenza, commonly called "the flu", is a respiratory illness caused by influenza type A or type B viruses. Typical symptoms of influenza include fever, respiratory symptoms (such as cough, sore throat, and other "cold" symptoms), muscle aches and headache. Most young, healthy people who get influenza recover completely within 1-2 weeks. Older people and those with certain chronic diseases are much more likely to develop serious medical complications or die following influenza.

Influenza is a particularly serious problem in nursing homes. Because of their age and health problems, nursing home residents are at high risk of developing serious complications or dying when they get influenza. They may also be at high risk of exposure to influenza, since the virus spreads more easily in environments where people live close to each other. Once the virus enters a nursing home, it can spread rapidly. During nursing home outbreaks more than half of the residents may be infected, and many may be hospitalized or die.

Influenza typically occurs annually in the winter between October and April; peak activity in a community usually lasts from 6 to 8 weeks, historically spanning the New Year period. These recommendations are being issued in anticipation of possible influenza outbreaks in California long-term care facilities this season. During the 1998-99 influenza season, both influenza A(H3N2) was the predominate virus detected in California. Although influenza activity was moderate, no outbreaks were reported in California long-term care facilities. Overall, the 1998-99 influenza vaccine strains were well matched with the circulating virus strains. An outbreak of influenza in Alaska this summer was of the same strain of influenza A(H3N2) that has been present for the past three years. The 1999/2000 vaccine will provide protection against this strain, although outbreaks can still occur among vaccinated groups. When feasible, measures should be taken to reduce contact between symptomatic and asymptomatic persons during outbreaks. In addition, chemoprophylaxis with rimantadine or amantadine should be considered during influenza A outbreaks in nursing homes. These drugs can also be used for treatment as they can reduce the severity and shorten the duration of influenza A illness when treatment is initiated within 48 hours of illness onset.

How Is Influenza Transmitted?

Influenza is spread from person-to-person by large droplets of respiratory secretions from an infected person coming into direct contact with the upper respiratory tract (nose, throat) of an uninfected person. It is also transmitted by inhalation (breathing in) of small droplets that are expelled into the air by an infected person, particularly when coughing. Transmission may also occur by contact with hands or environmental surfaces contaminated with virus, and then transferring the virus to the upper respiratory tract, but these are probably of limited importance. The most important sources of influenza virus are infected persons, and the period of greatest communicability is during the first 3 days of illness; however, the virus can be shed for 1 day before onset of symptoms and up to 7 or more days after illness onset.

How Is Influenza Diagnosed?

A person with influenza may not appear or feel different than when infected with many other respiratory illnesses that cause fever. When an outbreak of influenza-like illness begins in a nursing home, the local health department and licensing programs should be notified. Health department personnel can provide information about influenza activity in the area and about how to collect specimens and get a diagnosis. Rapid diagnostic tests allow early diagnosis and treatment of cases of type A influenza. These can be performed on nasopharyngeal-swab or nasal-wash specimens. This information can then be used to begin the use of antiviral drugs to prevent the outbreak from spreading. Precise identification of the strain of virus can be made by growing the virus from nasopharyngeal secretions of acutely ill persons. During outbreaks with laboratory-confirmed cases, persons with similar illnesses can be presumed to also have influenza.

How Can Influenza Outbreaks Be Detected?

Nursing homes should have a system for monitoring the incidence (number of cases over a period of time) of respiratory illness with fever among residents and staff. For this purpose, influenza-like illness is often defined as fever higher than 99.8°F orally or 100.8°F rectally and at least one of the following: cough, sore throat or "cold" symptoms (such as nasal congestion). An outbreak is when the incidence exceeds that which is expected. Since early detection of outbreaks of influenza is so important and assistance in the diagnosis of influenza may be needed, nursing home should consider notifying local health departments when 2-3 or more cases of influenza-like illness occur in a week in residents or staff.

How Can Influenza Be Prevented?

Vaccination of persons at high risk for complications of influenza is currently the most effective measure for reducing the illness and deaths from influenza, and should be done each year before the influenza season. When over 60% of residents of a long-term care facility are vaccinated, the risk of outbreaks is reduced. Vaccination should be routinely provided to all residents of nursing home with the blanket agreement of attending physicians on file rather than by obtaining individual vaccination orders for each resident. Consent for vaccination should similarly be obtained from the resident or a family member at the time of admission to the facility, and all residents and staff should be vaccinated in the fall. Residents admitted during the winter months should be vaccinated when they are admitted.

How Can Antiviral Agents Be Used For Influenza?

When a nursing home outbreak is due to influenza A, antiviral agents can be used for treatment of ill persons and for prophylaxis of others. Two related antiviral agents, amantadine hydrochloride and rimantadine hydrochloride, are effective against influenza-A, but not influenza-B, virus. These agents can be used

(1) for short-term prophylaxis (up to 14 days after vaccination) after late vaccination of high-risk persons;

(2) as prophylaxis for persons for whom vaccination is contraindicated;

(3) as prophylaxis for immunocompromised persons who may not produce protective levels of antibody in response to vaccination;

(4) as prophylaxis for unvaccinated healthcare workers who provide care to high-risk patients while there is influenza activity in the community or until immunity develops after vaccination;

(5) when vaccine strains do not closely match the epidemic viral strain; and

(6) as treatment of type A influenza, if started within 48 hours of illness onset.

Amantadine and rimantadine can protect against all naturally occurring strains of type A influenza virus; thus, antigenic changes in the virus that could reduce vaccine efficacy do not alter the effectiveness of amantadine or rimantadine. Both are 70-90% effective in preventing illness if taken before exposure to influenza A virus. In addition, they lessen the severity and duration of illness due to influenza A when administered within 24-48 hours after onset of symptoms. They can limit spread of influenza A in a nursing home if administered to all or most residents at the time influenza is recognized in a facility.

Side effects from amantadine are more common than those from rimantadine; they include mild and transitory nervousness, insomnia, impaired concentration, mood changes, light-headedness, anorexia, and nausea. These symptoms have been reported in 5-10% of healthy young adults receiving 200 mg of the drug per day. In the elderly, the symptoms can be more severe; in addition, dizziness and ataxia are more common in this age group. Thus, it is recommended that for persons $\geq$65 years of age and/or those who have renal insufficiency, amantadine dosage should be reduced to 100 mg per day. Further reductions are recommended on the basis of the patient's creatinine clearance. However, because recommended dosages based on creatinine clearance may provide only a rough estimate of the optimal dose for a given patient, such persons should be carefully observed so that adverse reactions can be recognized promptly and the dose further reduced or discontinued, if necessary. [See Appendix A for doses]

When amantadine or rimantadine is administered as prophylaxis, cost, compliance, and potential side effects should be considered when determining the period of prophylaxis. To be maximally effective as prophylaxis, the drug must be taken each day for the duration of influenza activity in the facility. Emergence of amantadine- and rimantadine-resistant strains of influenza A virus can occur in persons receiving these drugs for treatment of infection. Resistant viral strains could then be transmitted to their close contacts. Therefore, treatment for illness should be discontinued as soon as clinically warranted, generally after 3-5 days or within 24-48 hours after disappearance of acute signs and symptoms. To the extent possible, infected persons taking either drug should avoid contact with others during treatment and for 2 days after discontinuing treatment, particularly if the contacts are uninfected persons taking amantadine or rimantadine for prophylaxis.

When outbreaks of influenza A occur in a long-term care facility, and antiviral prophylaxis of high-risk persons and treatment of cases is undertaken, administration of amantadine or rimantadine should begin as early in the outbreak as possible to reduce transmission. Contingency planning is needed to ensure immediate availability and rapid administration of rimantadine or amantadine. This might include obtaining prior approval from personal physicians for administration of antiviral drugs to residents in the event of an outbreak. Since it is difficult to know in advance how long antiviral drugs will need to be administered, some nursing homes have a policy that also allows facility staff or a consultant to decide when they should be discontinued.

How Can New Antiviral Agents Be Used For Influenza?

A new type of influenza drug, called neuraminidase inhibitor, was recently developed. The advantage of these drugs is that they are effective against both influenza A and B, and the risk of development of resistance during treatment is low. Safety and effectiveness have not been established for their use in preventing influenza, so that during an outbreak they should be used only for treatment of symptomatic patients except under experimental study conditions.

One neuraminidase inhibitor, Relenza (zanamivir, Glaxo Wellcome), has been approved by the FDA for treatment of uncomplicated influenza. Administered by inhalation using a hand-held, breath-activated device called a Diskhaler within the first 2 days of symptom onset, Relenza reduces the duration of influenza-related symptoms. Relenza can cause bronchospasm in patients with asthma, so that it should be used with caution in patients with asthma or chronic obstructive pulmonary disease. A second neuraminidase inhibitor, an oral drug called Tamiflu (oseltamivir, Roche) has been submitted to the FDA for approval, and may be available for treatment of acute influenza by this winter.

What Else Can Be Done During Influenza Outbreaks?

Measures other than vaccination and chemoprophylaxis with amantadine or rimantadine have been recommended for control of nosocomial influenza outbreaks. Because influenza can be transmitted during contact with an infected person, contact-isolation precautions, such as placing a patient symptomatic with influenza in a private room, cohorting of patients with influenza, and masking upon entering a room with persons with influenza have been recommended. Handwashing, gloving, and gowning by healthcare workers during the period of viral shedding by patients have also been recommended. The following additional measures have also been recommended for consideration, particularly during severe outbreaks: (1) curtailment or temporary closure of facility to new admissions; (2) restriction of visitors, especially those with acute respiratory illnesses; and (3) work restriction for healthcare workers with acute respiratory illness.

Recommendations for Control of Influenza Outbreaks

A. Determine the Outbreak Strain

Early in the outbreak, obtain nasopharyngeal-swab or nasal-wash specimens from patients with symptoms suggestive of influenza for influenza virus culture or antigen detection.

B. Vaccinate Patients and Personnel

Administer current influenza vaccine to unvaccinated patients and staff, especially if the outbreak occurs early in the influenza season.

C. Amantadine or Rimantadine Administration

1. When a nosocomial outbreak of influenza A is suspected or recognized:
   a. Administer amantadine or rimantadine as prophylaxis to all uninfected patients in the involved unit for whom it is not contraindicated. Do not delay administration of amantadine or rimantadine unless the results of diagnostic tests to identify the infecting strain(s) can be obtained within 12 to 24 hours after specimen collection.
   b. Administer amantadine or rimantadine for prophylaxis to unvaccinated staff members for whom it is not medically contraindicated and who are in the involved unit or taking care of high-risk patients.
2. Discontinue amantadine or rimantadine if laboratory tests confirm or strongly suggest that influenza type A is not the cause of the outbreak.
3. If the cause of the outbreak is confirmed or believed to be influenza type A AND vaccine has been administered only recently to susceptible patients and personnel, continue amantadine or rimantadine prophylaxis until 2 weeks after the vaccination.
4. To the extent possible, do not allow contact between those at high risk of complications from influenza and patients who are taking amantadine or rimantadine for <u>treatment</u> of acute respiratory illness; prevent contact during and for two days after the latter discontinue treatment.

D. Interruption of (Person-to-Person) Transmission

1. Keep a patient for whom influenza is suspected or diagnosed in a private room, or in a room with other patients with proven influenza unless there are medical contraindications.
2. As much as feasible place together persons with influenza-like illness in an area with an independent air supply and exhaust system.
3. Institute masking of individuals who enter the room of a patient with influenza.
4. As much as possible during periods of influenza activity in the community, remove patient-care staff who have symptoms of febrile respiratory tract infection suggestive of influenza from duties that involve direct patient contact.
5. When outbreaks are characterized by high attack rates and severe illness:
   a. Restrict visitors who have a febrile respiratory illness.
   b. Curtail or temporarily close facility to new admissions as necessary.

APPENDIX A. Recommended dosage and duration for amantadine and rimantadine treatment and prophylaxis of influenza A in adults in long-term care facilities.

Dosage

	Age (yrs)	
Antiviral agent	**14-64**	**≥65**
Amantadine[1]	100 mg twice daily	≤100 mg/day
Rimantadine[2]	100 mg twice daily	100 mg/day

[1]The drug package insert should be consulted for dosage recommendations for administering amantadine to persons with creatinine clearance ≤50mL/min/1.73m^2

[2]A reduction in dose to 100mg/day of rimantadine is recommended for persons who have severe hepatic dysfunction or those with creatinine clearance ≤10mL/min. Other persons with less severe hepatic or renal dysfunction taking >100mg/day of rimantadine should be observed closely, and the dosage should be reduced or the drug discontinued, if necessary.

Duration

Prophylaxis	For the duration of influenza activity in the facility or until 14 days have passed following the administration of influenza vaccine, if possible. Factors such as cost, compliance, and potential side effects should be considered.
Treatment of Influenza-like Illness	3-5 days or discontinue within 24-48 hours after disappearance of acute signs and symptoms.

REFERENCES

Centers for Disease Control and Prevention (CDC). Prevention and Control of Influenza. Recommendations of the Advisory Committee on Immunization Practices (ACIP). Morbidity and Mortality Weekly Report (MMWR) April 30, 1999, Vol. 48, No. RR-4.

The Department encourages infection control committees to review these recommendations. Questions regarding the use of antiviral agents should be directed to Jon Rosenberg M.D., Division of Communicable Diseases at (510) 540-3233. Questions regarding infection control issues should be directed to Ms. Chris Cahill, Licensing and Certification at (916) 327-4330. Written comments about the information contained in these recommendations should be addressed to Chris Cahill, Infection Control Consultant, Department of Health Services, Licensing and Certification, 1800 3rd Street, Suite 210, PO Box 942732, Sacramento, CA 94234-7320.